FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 17:49:10 ON 16 FEB 2006

L1 70936 S (LEADER PEPTIDE) OR (SIGNAL SEQUENCE) OR (SIGNAL PEPTIDE)
L2 388 S L1 (P) ADENOVIR?
L3 98 S L2 AND ("E3" OR "E19")
L4 37 DUP REM L3 (61 DUPLICATES REMOVED)
L5 21 S L4 AND PY<=1999
L6 58 S L1 (S) ENDOSTATIN
L7 28 DUP REM L6 (30 DUPLICATES REMOVED)
L8 0 S L7 AND PY<=1999
L9 108 S L1 (P) (ENDOSTATIN OR ANTIANGIOGENIC OR ANTI-ANGIOGENIC)
L10 53 DUP REM L9 (55 DUPLICATES REMOVED)
L11 7 S L10 AND PY<=1999
L12 276 S (ENDOSTATIN OR ANTIANGIOGENIC OR ANTI-ANGIOGENIC) (S) ADENOVI
L13 16 S L12 AND L1
L14 11 DUP REM L13 (5 DUPLICATES REMOVED)

IN Restifo, Nicholas P.; Rosenberg, Steven A.; Bennink, Jack R.; Bacik, Igor; Yewdell, Jonathan W.
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
TI Immunogenic chimeras comprising endoplasmic reticulum signal peptide and an immunogenic peptide and their uses in vaccines and disease treatments
AB An immunogenic chimera comprising an endoplasmic reticulum (ER) signal peptide of gene E3/19K of adenovirus 5 and .gtoreq.1 other peptide is disclosed. A recombinant vaccinia virus construct capable of directing host organism synthesis of immunogenic chimeric proteins which can be used as immunogens, as vaccines, or in methods of treatment for cancer, infectious diseases, or autoimmune diseases is also prepd. The efficacy on eliciting a T-cell response of recombinant vaccinia virus VV-ES NP 147-155 encoding the ER signal peptide fused with the 9-amino-acid min. determinant of nucleopeptide of the influenza virus A/Puerto Rico/8/34 was demonstrated.

AU Persson H; Jornvall H; Zabielski J
SO Proceedings of the National Academy of Sciences of the United States of America, (1980 Nov) 77 (11) 6349-53.
Journal code: 7505876. ISSN: 0027-8424.
TI Multiple mRNA species for the precursor to an adenovirus-encoded glycoprotein: identification and structure of the signal sequence.
AB Early region 3 of the adenovirus type 2 genome encodes three proteins with molecular weights of 16,000, 14,500, and 14,000 (E2/16, E3/14.5, and E3/14). The E3/16 protein is the precursor to the E3/19 glycoprotein and is around 1500 daltons larger than the unglycosylated E3/190 protein. The E3/14.5 and E3/14 proteins are structurally related to each other but different from E3/16. Three mRNA species were identified for E3/16; all have common 5' ends with the same spliced region but with different 3' ends. E3/14 was translated from a 13S mRNA with the same 5' structure as the E3/16 mRNA but followed by a second spliced region with a different 3' end. A partial amino acid sequence was determined for E3/16 after radioactive labeling in vitro and this sequence can be aligned with a known DNA sequence. It contains a hydrophobic signal sequence, two presumptive glycosylation sites, and a hydrophobic region close to the COOH terminus.

AU Wold W S; Cladaras C; Deutscher S L; Kapoor Q S
SO Journal of biological chemistry, (1985 Feb 25) 260 (4) 2424-31.
Journal code: 2985121R. ISSN: 0021-9258.
TI The 19-kDa glycoprotein coded by region E3 of adenovirus.

Purification, characterization, and structural analysis.

AB The 19-kDa glycoprotein (gp 19K) coded by early region E3 of adenovirus is of interest as a model for glycoprotein processing and sorting, as well as for the interaction between viral antigens and class I transplantation antigens. In this paper, we show that gp 19K is a major protein synthesized during early stages of infection of human KB cells. We report the purification of gp 19K to near homogeneity, the preparation of a gp 19K antiserum, and structural analyses on the protein. We have determined the DNA sequence of the gp 19K gene in adenovirus type 5 (Ad5) for comparison with the published sequence (Herisse, J., Courtois, G., and Galibert, F. (1980) Nucleic Acids Res. 8, 2173-2192) of adenovirus type 2 (Ad2). Fragments produced by cyanogen bromide cleavage of Ad2 gp 19K are in accord with the DNA sequence, as are synthetic peptide antibodies targeted to the NH2 terminus of Ad2 gp 19K and the COOH terminus of Ad5 gp 19K. The Ad2 and Ad5 proteins are quite homologous. Conserved features include an NH2-terminal signal sequence, two potential Asn-linked glycosylation sites, and a 20-residue putative transmembrane hydrophobic domain followed by a 15-residue polar domain at the COOH terminus. We show that cleavage of the signal peptide occurs between the 17th and 18th amino acids on both the Ad2 and Ad5 versions of gp 19K and that both potential sites are glycosylated with exclusively high-mannose (as opposed to complex) oligosaccharides. Secondary structure predictions suggest six alpha-helix regions including the signal peptide and transmembrane domain, two or three beta-sheet regions, and about eight beta-turns including the two glycosylation sites and the regions flanking the transmembrane domain.

AU Krajcsi P; Tollefson A E; Anderson C W; Stewart A R; Carlin C R; Wold W S

SO Virology, (1992 Mar) 187 (1) 131-44.
Journal code: 0110674. ISSN: 0042-6822.

TI The E3-10.4K protein of adenovirus is an integral membrane protein that is partially cleaved between Ala22 and Ala23 and has a Ccyt orientation.

AB The Ad2 E3-10.4K protein is required together with the E3-14.5K protein to down-regulate the epidermal growth factor receptor in adenovirus-infected cells. Both proteins are also required to prevent tumor necrosis factor cytolysis under certain conditions. 10.4K is a 91 amino acid membrane-associated protein that migrates as two bands, upper and lower, on SDS-PAGE. We show here that the upper band is the primary translation product which initiates at AUG2173 in the E3 transcription unit of Ad2. The upper band is processed slowly (greater than 4 hr to complete) into the lower band by proteolytic cleavage between residues Ala22 and Ala23 by a microsome-associated protease. The upper and lower bands become equal in abundance, after which they are very stable. The N-terminus of the in vivo-derived upper band is not blocked to sequencing and it retains its initiating Met. 10.4K has a hydrophobic domain (H1) near its N-terminus that is probably a signal sequence for membrane insertion; cleavage of this signal is atypical because it was not cotranslational in vivo and it was not complete. 10.4K has a second hydrophobic domain (H2) located within residues 35-60. H2 appears to be a transmembrane (stop transfer) domain because both the upper and the lower 10.4K bands remained associated with membranes after extraction at pH 11.5, because both bands were extracted into the detergent phase with Triton X-114, and because both bands were only partially reduced in size when 10.4K-containing microsomes were digested with proteinase K. These proteinase K-digested bands were immunoprecipitated with an antipeptide antiserum against residues 19-34 but not with an antiserum against residues 68-80 or 77-91, indicating that both 10.4K bands are orientated in the membrane with the C-terminus in the cytoplasm. We conclude that the lower band of 10.4K is a type I bitopic membrane protein and suggest that the upper band is a polytopic membrane protein with both the H1 and

the H2 hydrophobic domains spanning the membrane.

AU Lawson C M; Bennink J R; Restifo N P; Yewdell J W; Murphy B R
SO Journal of virology, (1994 Jun) 68 (6) 3505-11.
Journal code: 0113724. ISSN: 0022-538X.
TI Primary pulmonary cytotoxic T lymphocytes induced by immunization with a vaccinia virus recombinant expressing influenza A virus nucleoprotein peptide do not protect mice against challenge.
AB The nucleoprotein (NP) of influenza A virus is the dominant antigen recognized by influenza virus-specific cytotoxic T lymphocytes (CTLs), and adoptive transfer of NP-specific CTLs protects mice from influenza A virus infection. BALB/c mouse cells (H-2d) recognize a single Kd-restricted CTL epitope of NP consisting of amino acids 147 to 155. In the present study, mice were immunized with various vaccinia virus recombinant viruses to examine the effect of the induction of primary pulmonary CTLs on resistance to challenge with influenza A/Puerto Rico/8/34 virus. The minigene ESNP(147-155)-VAC construct, composed of a signal sequence from the adenovirus E3/19K glycoprotein (designated ES) and expressing the 9-amino-acid NP natural determinant (amino acids 147 to 155) preceded by an alanine residue, a similar minigene NP(Met 147-155)-VAC lacking ES, and a full-length NP-VAC recombinant of influenza virus were analyzed. The two minigene NP-VAC recombinants induced a greater primary pulmonary CTL response than the full-length NP-VAC recombinant. However, NP-specific CTLs induced by immunization with ESNP(147-155)-VAC did not decrease peak virus titer or accelerate clearance of virus in the lungs of mice challenged intranasally with A/PR/8/34. Furthermore, NP-specific CTLs induced by immunization did not protect mice challenged intranasally with a lethal dose of A/PR/8/34. Sequence analysis of the NP CTL epitope of A/PR/8/34 challenge virus obtained from lungs after 8 days of replication in ESNP(147-155)-VAC-immunized mice showed identity with that of the input virus, demonstrating that an escape mutant had not emerged during replication in vivo. Thus, in contrast to adoptively transferred CTLs, pulmonary NP-specific CTLs induced by recombinant vaccinia virus immunization do not have protective in vivo antiviral activity against influenza virus infection.

AU Zajac P; Oertli D; Spagnoli G C; Noppen C; Schaefer C; Heberer M; Marti W R
SO International journal of cancer. Journal international du cancer, (1997 May 2) 71 (3) 491-6.
Journal code: 0042124. ISSN: 0020-7136.
TI Generation of tumoricidal cytotoxic T lymphocytes from healthy donors after in vitro stimulation with a replication-incompetent vaccinia virus encoding MART-1/Melan-A 27-35 epitope.
AB Active specific immunotherapy targeting tumor-associated antigens (TAA) requires reagents of high immunogenicity and safety. To address this issue, we constructed a recombinant vaccinia virus carrying a minigene insert encoding the HLA-A2.1-restricted MART-1/Melan-A27-35 melanoma TAA (rVV-M). To facilitate the entry of the antigenic epitope into the endoplasmic reticulum, a sequence coding for adenovirus E3/19K leader peptide was added. This rVV-M was made replication-incompetent by treatment with psoralen and UV light. Infection with rVV-M rendered HLA-A2.1 EBV-transformed lymphoblastoid cells sensitive to the cytotoxic effects of HLA-class-1-restricted, MART-1/Melan-A27-35-specific cytotoxic T lymphocytes (CTL). The capacity of rVV-M to generate HLA-A2.1-restricted MART-1/Melan A-specific CTL was demonstrated from tumor-infiltrating-lymphocyte (TIL) cultures and from healthy donors' peripheral-blood mononuclear cells (PBMC). MART-1/Melan-A27-35-specific CTL were generated from TIL after 2 weekly stimulation courses. Infection with rVV-M elicited a higher CTL response than addition of exogenous peptide, whereas, when a similar protocol was used to stimulate PBMC of healthy donors, significant and specific

cytotoxic activity could be observed only upon rVV-M infection but not upon exogenous peptide addition. All CTL generated upon rVV-M stimulation were also able to efficiently kill melanoma cell lines expressing both MART-1/Melan-A and HLA-A2.1. In addition, TNF-alpha production could be induced in rVV-M-stimulated CTL upon co-culture with COS-7 cells transiently transfected with MART-1/Melan-A and HLA-A2.1 genes. This safe and highly immunogenic reagent could be of use in TAA-targeted clinical immunotherapy.

IN Libutti, Steven K.; Feldman, Andrew
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2.
TI Systemic gene therapy of tumors with genes for angiogenesis inhibitors to prevent tumor vascularization
AB This invention provides a compd. comprising a recombinant nucleic acid encoding an antiangiogenic protein inserted within a viral nucleic acid, wherein the recombinant nucleic acid can be packaged in a virus particle and wherein expression of the recombinant nucleic acid encoding the antiangiogenic protein results in prodn. of the antiangiogenic protein. The present invention also provides a method of delivering an antiangiogenic protein to a cell, delivering an antiangiogenic protein to a subject, and treating a tumor in a subject comprising administering a virus comprising a recombinant nucleic acid encoding an antiangiogenic protein inserted within the viral nucleic acid, wherein the recombinant nucleic acid can be packaged in a virus particle, and wherein expression of the recombinant nucleic acid encoding the antiangiogenic protein results in prodn. of the antiangiogenic protein, thereby delivering the antiangiogenic protein to the cell. The use of adenovirus vectors carrying secretory expression constructs for human and mouse endostatin is demonstrated. The adenovirus E3/19k signal sequence was used. A signal peptide was necessary to ensure efficient secretion of the endostatin into the medium. The conditioned medium effectively inhibited the proliferation of microvascular cells in vitro. The secretory expression vector also raised serum endostatin levels in nude mice and no adverse effects of the virus were seen with inocula of 109 pfu. Serum endostatin levels peaked 4 days after inoculation. Mice carrying the endostatin secretory expression construct showed slower growth of implanted tumors than did control animals.

AU Mori, Keisuke; Ando, Akira; Gehlbach, Peter; Nesbitt, David; Takahashi, Kyoichi; Goldsteen, Donna; Penn, Michael; Chen, Cheauyan T.; Mori, Keiko; Melia, Michele; Phipps, Sandrina; Moffat, Diana; Brazzell, Kim; Liau, Gene; Dixon, Katharine H.; Campochiaro, Peter A. [Reprint author]
SO American Journal of Pathology, (July, 2001) Vol. 159, No. 1, pp. 313-320. print.
CODEN: AJPAA4. ISSN: 0002-9440.
TI Inhibition of choroidal neovascularization by intravenous injection of adenoviral vectors expressing secretable endostatin.
AB Endostatin is a cleavage product of collagen XVIII that inhibits tumor angiogenesis and growth. Interferon alpha2a blocks tumor angiogenesis and causes regression of hemangiomas, but has no effect on choroidal neovascularization (CNV). Therefore, inhibitors of tumor angiogenesis do not necessarily inhibit ocular neovascularization. In this study, we used an intravenous injection of adenoviral vectors containing a sig-mEndo transgene consisting of marine immunoglobulin kappa-chain leader sequence coupled to sequence coding for marine endostatin to investigate the effect of high serum levels of endostatin on CNV in mice. Mice injected with a construct in which sig-mEndo expression was driven by the Rous sarcoma virus promoter had moderately high serum levels of endostatin and significantly smaller CNV lesions at sites of

laser-induced rupture of Bruch's membrane than mice injected with null vector. Mice injected with a construct in which sig-mEndo was driven by the simian cytomegalovirus promoter had apprx10-fold higher endostatin serum levels and had nearly complete prevention of CNV. There was a strong inverse correlation between endostatin serum level and area of CNV. This study provides proof of principle that gene therapy to increase levels of endostatin can prevent the development of CNV and may provide a new treatment for the leading cause of severe loss of vision in patients with age-related macular degeneration.